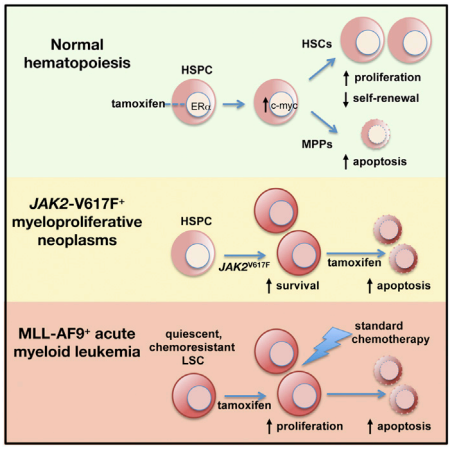
In This Issue



Stem Cell Energetics

VOICES, 679

Growing evidence shows that cellular metabolism is a key determinant of stem cell fate. In recognition of this growing area of research, *Cell Stem Cell* and *Cell Metabolism* have teamed up with academic co-organizers Drs. Emmanuelle Passegué and Michael Teitell for our upcoming Cell Symposium, Stem Cell Energetics, which takes place December 9th –11th, 2014. In anticipation of the meeting, we asked speakers to discuss what drives them to study this topic, including key findings and burning questions. In a Voices piece that appears in this issue (and the December 2, 2014 issue of *Cell Metabolism*), a selection of speakers share their thoughts.

The Journey from the Crypt to the Clinic

ZEUNER ET AL., 692

This Review presents a current understanding of colorectal CSCs, including their origin, relationship to stem cells of the intestine, phenotypic characterization, and underlying regulatory mechanisms. Limitations to current preclinical models of colorectal cancer and how understanding CSC plasticity can improve the development of clinical strategies are also covered.

M^{6}Arking ESCs for Differentiation

BATISTA ET AL., 707

N6-methyl-adenosine (m^{6}A) is the most abundant modification on messenger RNAs. Batista et al. show that core pluripotency factors are regulated by m^{6}A, and depletion of m^{6}A levels by inactivation of Mettl3 impairs ESC exit from self-renewal and blocks differentiation. Preview by Jalkanen and Wilusz.

Nucleolar Regulation of Pluripotency

SAVIĆ ET AL., 720 AND LEE ET AL., 735

Savić et al. show that heterochromatin condensation in the nucleolus, where ribosomal genes are transcribed, triggers remodeling of open ESC chromatin into a highly condensed heterochromatic structure and stimulates exit from pluripotency via activation of differentiation genes. Kim et al. reveal that LIN28A, which is methylated by SET7/9, multimerizes to sequester and prevent biogenesis of pri-let-7 in the nucleoli of hESCs, thereby modulating their pluripotency. Preview by Feinberg.

Using Estrogens to Target Leukemia

SÁNCHEZ-AGUILERA ET AL., 791

Activation of estrogen receptor (ER) signaling induces apoptosis in MPPs, but induces proliferation of HSCs, in a reversible manner. ER activation with tamoxifen blocks development of myeloproliferative neoplasm by restoring normal apoptosis levels in mutant cells and induces apoptosis of AML blasts, in combination with conventional chemotherapy. (Top image.)

Patching up Broken Hearts

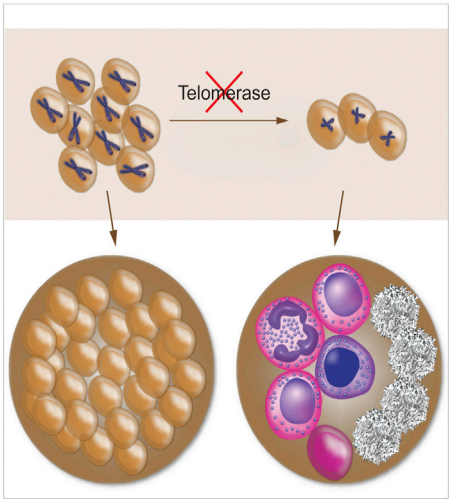
YE ET AL., 750

Engraftment of hPSC-derived cardiomyocytes, endothelial cells, and smooth muscle cells into a large animal model of myocardial infarction improves heart function and metabolism without inducing ventricular arrhythmias. Preview by Serpooshan and Wu.

Defeating LSCs by Depleting Telomerase

BRUEDIGAM ET AL., 775

Bruedigam et al. show that inhibiting telomerase in both mouse and human AML targets and depletes LSCs, impairs leukemic progression, and delays relapse after chemotherapy. Preview by Kuo and Bhatia. (Bottom image.)



Stromal MicroRNAs Promote Breast Cancer Metastasis

CUIFFO ET AL., 762

Repression of *FOXP2* by a network of mesenchymal-stem-cell-regulated microRNAs facilitates the acquisition of cancer stem cell and metastatic phenotypes by breast cancer cells.